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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 25

Application Number: 09/420,695
Filing Date: October 19, 1999
Appellant(s): Yasmin Thanavala, Charles Joel Arntzen, and Hugh S. Mason

Michael L. Dunn
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed July 30, 2001.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1 and 4-18 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

A substantially correct copy of appealed claim 7 appears on page 8 of the Appendix to the appellant's brief. The minor errors are as follows: There is an apparent misspelling in Claim 7, line 2, wherein it appears that the word "pant" should be replaced with the word - - plant - -.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5,935,570	Koprowski et al.	8/10/1999
5,914,123	Arntzen et al.	6/22/1999

Stites et al. Basic and Clinical Immunology. 7th ed. USA: Appleton & Lange. 1991. "Chapter 58: Immunization" by Grossman et al., pages 723-741 and page 102.

(10) Grounds of Rejection

The following ground of rejection is applicable to the appealed claims:

Claims 1 and 4-18 stand rejected under 35 U.S.C. § 103 as being unpatentable over Arntzen et al. (US Patent 5,914,123) in view of Koprowski et al. (US Patent 5,935,570) and

Stites et al. (Basic and Clinical Immunology. 7th ed. USA: Appleton & Lange. 1991. "Chapter 58: Immunization" by Grossman et al., pages 723-741 and page 102).

A method for providing a serum IgM and IgG response specific to hepatitis B surface antigen (HBsAg), in an animal by feeding the animal with a substance comprising a physiologically acceptable plant material containing hepatitis B antigen in combination with an adjuvant, said combination causing serum IgM and IgG responses specific to HBsAg in excess of serum IgM and IgG responses specific to HBsAg caused by HBsAg alone is claimed. Dependent claims recite administering plant material from a plant that has been genetically altered to express said antigen to an animal and/or human in therapeutic dose amounts over a plurality of different times, wherein the plant material is from a plant of the family *Solanaceae*, namely a potato or a tomato.

Arntzen teaches an anti-viral vaccine produced in physiologically acceptable plants, particularly the potato and the tomato, which is administered by feeding the plants to an animal or a human. Arntzen specifically teaches methods of making a transgenic plant expressing an immunogen derived from hepatitis B surface antigen, wherein the immunogen is capable of eliciting an immune response in a subject by consumption of said plant material. Finally, Arntzen teaches that the plurality of different administrations of the genetically altered plant material expressing HBsAg over separate periods of time will provide the claimed functional effect of raising the serum IgM and IgG response specific to HBsAg to achieve immunization of a mammal. Note that Arntzen specifically teaches that the plurality of times for the

administration of the vaccines is in a range of 3 to 6, and that the time separating the vaccinations is in a range of 14 to 84 days to achieve protective levels of antibodies (Column 15, lines 45-61). Arntzen does not teach a method for providing a serum IgM and IgG response specific to hepatitis B antigen in an animal by feeding the animal or human with a substance comprising a physiologically acceptable plant containing HBsAg in combination with an adjuvant. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the claimed invention by adding an adjuvant to the plant material taught by Arntzen because Koprowski and Stites teach the benefits of combining an adjuvant to a vaccine. For instance, Koprowski teaches a process for the genetic alteration of a microorganism such that it synthesizes an immunologic compound and produces an immunologic effect in an animal or human, when administered thereto. A plant may be infected may be infected with the genetically altered microorganism and used as an oral delivery vaccine system. The vaccine, if administered by the oral route, is done by feeding the subject a physiologically acceptable plant material expressing the immunogen (Column 5, lines 54-61). The vaccine can further comprise an adjuvant to facilitate or improve activity (Column 6, lines 33-36). Koprowski further teaches, in Column 8, lines 1-31, plant infecting microorganisms and physiologically acceptable solanaceous plant material that can be genetically altered to express an immunogen, including tuber material from the potato plant. Like Koprowski, Stites teaches that the response to an immunogen can be enhanced if it is administered as a mixture with an adjuvant. Moreover, Stites teaches methods for providing

immunological responses in an individual. At the time the invention was made, one of ordinary skill in the art would have been motivated to provide serum IgM and IgG responses specific to HBsAg in excess of serum IgM and IgG responses caused by HBsAg alone by combining an adjuvant to the composition taught by Arntzen because Koprowski and Stites provide the motivation and suggestion to provide the claimed invention. Thus, with Arntzen expressly teaching physiologically acceptable plant materials expressing hepatitis B surface antigen that could be used to both prime the mucosal immune system and/or stimulate the humoral immune response in a dose dependent manner, and with Koprowski teaching the oral delivery of plant material expressing a viral antigen in combination with an adjuvant, one of ordinary skill would have had a reasonable expectation of success to provide a method for providing the claimed functional effect of raising the serum IgM and IgG responses specific to HBsAg, wherein the response was greater than the response caused by HBsAg alone, because it was known in the art of immunology at the time the invention was made that the delivery of a vaccine in combination with an adjuvant facilitates and improves its immunological therapeutic activity in an individual, as evidenced by the teachings of both Koprowski and Stites.

It should be noted that as the references indicate the various proportions and amounts of the ingredient and the plurality of times for the administration of the ingredients over periods of time used in the claimed method are result variable, they would be routinely optimized by one of ordinary skill in the art practicing the invention disclosed by each of the references.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in providing the instantly claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence to the contrary.

(11) Response to Argument

Appellants argue that the claims are unobvious to one of skill in the art and patentable over the prior art of record because Arntzen neither teaches "methods of making a transgenic plant expressing an immunogen derived from hepatitis B surface antigen, wherein the immunogen is capable of eliciting an immune response in an animal by consumption of the plant material" nor provides supporting data showing any immune response whatsoever to the ingestion of tomato juice or any other plant material containing HBSAG. Appellant further argues that Arntzen does not teach how oral immunization to HBsAg might be accomplished using a transgenic plant, and that the plants made in the examples taught by Arntzen do not function orally to raise an immune response, as Arntzen alleges. Finally, Appellant argues that Koprowski neither teaches nor suggests any method for making a transgenic plant, and that Stites neither teaches nor suggests that the oral administration of HBSAG in the presence of a suitable adjuvant to an animal would effect a raise in the immune response. However, this is not found persuasive because the primary reference of Arntzen was relied upon because Arntzen clearly teaches an anti-viral vaccine

produced in physiologically acceptable plants, particularly the potato and the tomato, and then administered through standard vaccine procedure or by feeding the plants to an animal or a human. Arntzen specifically teaches methods of making a transgenic plant expressing an immunogen derived from hepatitis B surface antigen, wherein the immunogen is capable of eliciting an immune response in an animal by consumption of the plant material. Arntzen also teaches methods of making a vaccine by recovering the immunogen expressed in the plant cell for use as a vaccine. Moreover, Arntzen expressly teaches physiologically acceptable plant materials expressing HBSAG can be used both to prime the mucosal immune system and/or stimulate the humoral immune response in a dose dependent manner. See Column 3, lines 24, Columns 4-7 and Column 8, lines 1-21. In Column 11, lines 36-50, Arntzen teaches that either the parenteral or non-parenteral introduction of the vaccine to a mammal can elicit serum and/or secretory antibodies against the HBSAG immunogen of the vaccine with minimal induction of systemic tolerance. Finally, Arntzen teaches that a plurality of different administrations of the genetically altered plant material expressing HBSAG over separate periods of time will provide the claimed functional effect of raising the serum IgM and IgG response specific to the hepatitis B surface antigen to achieve immunization of a mammal. Note that Arntzen specifically teaches that the plurality of times for the administration of the vaccines is in a range of 3 to 6, and that the time separating the vaccinations is in a range of 14 to 35 days to achieve protective levels of antibodies. See Column 15, lines 45-61. The reference of Koprowski was primarily relied upon because Koprowski teaches a method of making transinfected plant material expressing a viral

antigen which can be used as an oral delivery system to elicit an immunologic effect in an animal or human; and, the reference of Koprowski clearly teaches that when the vaccine or therapeutic compound is delivered for immunologic purposes, it could be delivered with an adjuvant to facilitate or improve its immunological therapeutical activity. See Column 6, lines 22-36. Applicant argues that Koprowski does not suggest a specific adjuvant that would have the instantly claimed functional effect of raising the response of serum IgM and IgG responses specific to HBSAG, however the choice of adjuvant is not commensurate in scope to the limitations of the claimed invention. The reference of Stites was relied upon to demonstrate methods of providing immunological responses in an individual. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a serum IgM and IgG response specific to HBSAG by feeding an animal with a genetically altered plant expressing the hepatitis B surface antigen with an adjuvant, wherein the combination causes an excess of serum IgM and IgG than caused by HBSAG alone because both Arntzen and Koprowski teach that the oral delivery of genetically/and or transinfected plant material which express a viral antigen, such as the hepatitis B surface antigen taught by Arntzen, provide a positive humoral and/or mucosal immune responses when delivered to a mammal or human. At the time the invention was made, one of ordinary skill in the art would have been motivated to modify the method for the oral delivery of the composition taught by Arntzen by adding an adjuvant because Koprowski clearly teaches that the combination of plant material expressing a viral antigen and an adjuvant improves the immunological therapeutical activity of the drug. One

would have been further motivated with a reasonable expectation of success because it was well known in the art as taught by Stites that adjuvants enhance the response of an immunogen when the adjuvant is administered with the immunogen. See page 102. Thus, the results are no more than the mere combination of known drugs administered by very old and well known methods in the art of immunology because Arntzen, as well as Stites, teach that protective immunity can be effected by the multiple administration of a vaccine over a period of time; and therefore, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success that the instantly claimed method would provide the claimed functional immunological effect in an animal, wherein the animal was feed the drug combination.

It should be further noted that the various proportions and amounts of the ingredients, and the plurality of times for the administration of the ingredients over periods of time used in the claimed method are result variable, and as such they would be routinely optimized by one of ordinary skill in the art practicing the inventions disclosed by each of the references.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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October 9, 2001

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